

REMARKS

Claims 1-9, 11-12, 16-18, 23, and 34-44 are currently pending in the application. Claims 10, 13-15, 19-22, and 24-33 were withdrawn from consideration by the Examiner as non-elected claims, and have been canceled merely to comply with the Examiner's requirement to cancel non-elected subject matter. Applicant reserves the right to file one or more continuing applications drawn to the subject matter of such canceled claims. Claims 38-44 are new. It is understood that claims 18 and 23 are under consideration only to the extent that they read on the elected claims, i.e., Group I.

Amendments to the specification at the paragraphs beginning at page 8, line 17, and page 27, line 23, are made to correct spelling errors.

Claim amendments that substitute "species, genus, or family" for "species or group of related plant species" are supported at page 41, line 12, through, page 42, line 10.

Claim amendments that incorporate "diploid" are supported by claim 16.

Claim amendments that incorporate "angiospermous" are supported at page 62, lines 5-13.

Claims amendments that incorporate the concept that initiation of embryo sac formation occurs at about the same time or before

meiosis relative to developmental maturity of nongametophytic ovule and ovary tissues is supported at page 13, lines 8-21.

Claim 2 was amended to convert it from a Markush claim to a non-Markush claim. Claims 40-44 are new claims that incorporate the subject matter of original claim 2.

Thus, no new matter is added to the application by virtue of these amendments.

The application now contains 7 independent claims and 22 total claims. Applicant has previously paid excess claims fees for 7 or more independent claims and 22 or more total claims. Thus, no additional excess claims fees are due at this time. However, Applicant hereby authorizes the Commissioner to charge any deficiency or credit any overpayment concerning excess claims fees to Deposit Account No. 50-0836.

Applicant respectfully thanks the Examiner for withdrawing prior rejections based on 35 U.S.C. §§ 102 and 103. Applicants agree that claims 1-9, 11-12, 16-18, 23, and 34-37 are free of the prior art because the prior art fails to teach or suggest a method of producing apomictic plants from sexual plants based on breeding sexual plants that differ among lines in flowering responses to photoperiod and in start times and durations of female developmental stages in ovules. Applicant disagrees, however, with the Examiner's characterization that the presently claimed

invention is drawn to producing apomictic plants from sexual plants by hybridizing "any two sets of plant lines" wherein the plant lines differ in their flowering responses to photoperiods and their start times and durations of female or seed developmental stages and that enablement is lacking. Further comments about this issue will be presented below.

I. Written Statement as to Substance of Interview

Applicant respectfully thanks the Examiner for the courtesy extended to Applicant and the undersigned attorney in the personal interview held on March 28, 2003.

As required under MPEP § 713.04, a complete written statement as to the substance of the interview is now provided. Applicant acknowledges the Form PTO-413 filled out at the time of the interview.

(A) Brief Description of any Exhibit Shown or any Demonstration Conducted

Applicant presented a paper copy of a PowerPoint presentation including references cited therein. A Form 1449 containing a list of such references is enclosed herewith. The presentation related to the anatomy, evolution, and inheritance of apomixis; apomixis embryology; finding embryologically-divergent lines (especially

noting page 11); and breeding and selecting for apomixis (especially noting page 15).

(B) Identification of the Claims Discussed

Claims 1-37 were discussed in general. There was no specific discussion of any particular claim.

(C) Identification of Specific Prior Art Discussed

None.

(D) Identification of Principal Proposed Amendments Discussed

None.

(E) General Thrust of the Principal Arguments of the Applicant and the Examiner

Applicant summarized the invention and pointed out pages 11 and 15 of the PowerPoint presentation as being particularly illustrative of the timing of meiosis and embryo sac development in selected parent plants.

The Examiner stated that the claims were indefinite and that rejections under 35 U.S.C. § 112, paragraphs 1 and 2, would be largely or entirely obviated by amendment of the claims to reflect what the Applicant summarized in the interview as being the invention.

(F) General Indication of Other Pertinent Matters Discussed

None.

(G) General Results or Outcome

Applicant was to file a response to the Office Action of November 29, 2002, with amended claims.

II. Amendment of Claims to Delete Non-elected Material

The Examiner has required the Applicant to delete non-elected material from the elected claims and to delete non-elected claims. Applicant is herein complying with this requirement to further the prosecution of the application and in furtherance of receiving early allowance of the claims. However, Applicant makes the following observations.

There are two principal policies underlying a restriction requirement under 35 U.S.C. § 121. First, Section 101 has been interpreted to mean, in pertinent part, that a patent should contain claims drawn to only one invention. Second, restriction is appropriate such that the search and examination of a patent application is not unduly burdensome on an examiner. Neither of these policies is met by restricting the present application to a method for breeding diploid hybrid plant lines exhibiting apomixis.

With respect to the number of inventions in the present application, the ploidy level of the hybrid plants is irrelevant to the number of inventions in the application. If the parent lines are both diploid, then the hybrids will be diploid. If the parents are both tetraploid, then the hybrids will be tetraploid. If the

parents have differing ploidy levels, then the hybrids will have an intermediate ploidy level. The steps of the invention for selecting the parents and hybridizing them do not change depending on the ploidy level thereof, nor do the steps of the invention change depending on the ploidy level of the F1 hybrids. It is simply not a different invention to select diploid parents as opposed to selecting tetraploid parents or parents of other ploidy levels. Neither is it a different invention to obtain diploid hybrids or polyploid hybrids. Therefore, the requirement to restrict claims based on the ploidy of the hybrids is ill-conceived vis-a-vis the policy of having one invention per patent.

With respect to the burden on the Examiner to search and examine the application, the ploidy levels of the hybrids is also irrelevant to whether such search and examination is unduly burdensome. The vast majority of references applicable to this application are scientific papers. Scientific papers are not classified according to the patent classification system used by the PTO. Therefore, in searching the scientific literature for papers relating to apomictic diploid hybrids, the Examiner has simultaneously and unavoidably searched the scientific literature relating to apomictic hybrids of other ploidy levels. Applicant also suspects that the search of the patent literature also necessarily and unavoidably searched patents relating to apomictic

hybrids of all ploidy levels. Therefore, the requirement to restrict claims based on the ploidy of the hybrids is ill-conceived vis-a-vis the policy of not overburdening the Examiner.

Moreover, the restriction requirement is unduly burdensome to the Applicant. It will be unduly expensive and time-consuming to file numerous divisional applications to cover the territory to which Applicant believes he is entitled to patent protection. It is unfair to the Applicant for the PTO to require limitation of the scope of the claims when the restriction requirement makes no sense scientifically and does not further the policies that the restriction requirement is supposed to advance.

In view of these arguments, if the Examiner is persuaded that the restriction requirement is illogical and unfair, Applicant respectfully requests that the Examiner rejoin non-elected subject matter to the present application, at least to the extent that it relates to the ploidy level of the apomictic hybrids. Applicant will gladly restore the claims limited to diploid hybrids to claims that encompass all ploidy levels.

### III. Response to Objection to Disclosure

The Examiner objected to the disclosure for an alleged informality embodied as a horizontal line at page 62, line 10. Applicant has directed that this line be deleted. Therefore, the

objection is obviated, and withdrawal of the objection is respectfully requested.

#### IV. Priority

The present application is a continuation of U.S. Serial No. 09/018,875, filed February 5, 1998, now abandoned, which claims the benefit of U.S. Provisional Application No. 60/037,211, filed February 5, 1997. The Examiner has alleged that the present application is not entitled to priority to U.S. Provisional Application No. 60/037,211 (hereinafter, "the '211 provisional application"), and the corresponding filing date of February 5, 1997. The basis for this allegation is the Examiner's allegation that the '211 provisional application fails to provide enabling support for the presently claimed invention.

Applicant respectfully disagrees with the position taken by the Examiner and maintains the argument presented in paper no. 14 filed September 9, 2002.

Further, the '211 provisional application states in several places that asynchronous expression of genes responsible for female development is responsible for apomixis. For example, at page 22 the '211 provisional application states as follows:

When embryo sac development signals from one genome are superimposed on megasporogenesis signals from another genome, meiosis is skipped (diplospory) or embryo sac

development is ectopic (apospory). Accordingly, apomictic tendencies in hybrids or amphiploids will occur only if major differences in timing of meiosis, embryo sac development, and embryo formation exist between parental species.

At page 56 it further states that "diplospory is caused by a delicate balance of asynchronously-expressed developmental genes such that embryo sac signals from one genome are precociously-expressed with megasporogenesis signals from another genome." Other examples of this teaching could but cited. A teaching with respect to the role of photoperiodism is found at page 16, wherein it is stated that "[a]pomictic . . . species tended to occur together in cosmopolitan families in which temporal variation in female development is expected . . . ." Cosmopolitan genera and families are distributed across widely varying latitudes and habitats, and they are represented by numerous ecotypes, each of which is adapted to a specific habitat that is well within the broader distribution of the genus or family. By extension, apomictic plants evolved by secondary-contact hybridization between lines adapted to different latitudes. High-latitude plants are known in the art to generally be long day plants. Lower-latitude plants are known in the art to generally be either long day plants with a shorter day-length requirement for flowering than those typically found in higher latitudes, day neutral plants, or short day plants. Salisbury & Ross at 504-514.

The presently claimed invention reiterates the requirements to hybridize plants that differ in their flower initiation requirements and ovule development schedules as taught in these respective sections of the '211 application.

Applicant respectfully requests that the Examiner recognize on the record that the present application is entitled to priority to U.S. Provisional Application No. 60/037,211

V. Claim Objections

Claims 5-6, 8, and 18 were objected to for alleged informalities in these claims.

Claims 5-6, 8, and 18 have been amended herein for addressing these objections. Claims 5 and 6 have been canceled. Claim 8 has been amended to insert the article "the" before "nongametophytic." Claim 18 has been amended to delete the underlined comma and replace it with a non-underlined comma. Accordingly, withdrawal of these objections is respectfully requested.

VI. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-9, 11-12, 16-18, 23, and 34-37 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

The second paragraph of 35 U.S.C. § 112 is directed to requirements for the claims:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

There are two separate requirements set forth in this paragraph:

(1) the claims must set forth the subject matter that the applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

MPEP § 2171.

With respect to the second of these requirements:

The examiner's focus during examination of claims for compliance with the requirement for definiteness . . . is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. . . . [The examiner] should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. . . . The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. If the scope of the invention sought to be patented cannot be determined from the language of the claims with a reasonable degree of certainty, a rejection of the claims under 35 U.S.C. 112, second paragraph is

appropriate. In re Wiggins, 488 F.2d 538, 179 USPQ 421 (CCPA 1973).

MPEP § 2173.02 (emphasis in original); In re Moore, 169 U.S.P.Q. 236, 238 (C.C.P.A. 1971); Hybritech Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986); Shatterproof Glass Corp. v. Libbey Owens Ford Co., 225 U.S.P.Q. 634, 641 (Fed. Cir. 1985).

With that background in mind, the rejection of claims under 35 U.S.C. § 112, second paragraph, will now be discussed.

Claims 1, 17-18, and 34-37 were rejected for allegedly being indefinite for reciting "from sexual plants," "from sexual . . . plants," or "from . . . sexual plants." The Examiner alleged that these phrases are unclear as to whether or not the sexual plants are ones that normally only reproduce sexually or if facultative apomicts are intended to be included. Applicant respectfully submits that the claims are clear when the claims are read in light of the specification, as the appropriate guidelines direct. Facultative apomicts were not intended to be included. "Sexual plants," as used in the application, are plants that normally only reproduce sexually. At page 1, lines 6-8, the specification states: "This invention relates to methods for producing plants that genetically clone themselves through their own seed (gametophytic apomicts) from plants that normally reproduce

sexually." At page 12, lines 20-22, the specification states: "It is an object of the present invention to provide methods for creating apomictic plants from sexual plants without using mutagenic procedures or plants that are already apomictic." At page 38, lines 13-15, the specification states: "The present invention is directed to processes for producing gametophytic apomicts (plants expressing apospory or diplospory) from plants that typically undergo normal sexual reproduction." Numerous other statements in the specification also state that the present invention is directed to producing apomictic plants by hybridizing sexual parent plants. Therefore, a person skilled in the art would understand that when the claims refer to sexual plants, such sexual plants are plants that normally undergo sexually reproduction and not facultative apomicts.

The Examiner alleged that "environment causes apospory in many plants," citing the Evans and Hussey articles for support. This is a misinterpretation of what Evans and Hussey teach. These articles most definitely do not teach that environment causes apospory. In the abstract of the article, Evans states (emphasis added):

Two races were wholly sexual in their breeding system and two appeared to be almost entirely aposporous, but most were versatile, displaying both sexual and aposporous reproductive behaviour. In seven races there was some evidence that day length influenced the reproductive pathway, short days causing increased apospory in all

cases, regardless of the day length requirements for flowering.

Therefore, Evans does not teach that environment causes apospory. On the contrary, Evans teaches that environment can influence the expression of apospory, i.e., changing the level of apomixis expression from one level to another. In other words, Evans does not teach that environment can change an obligately sexual plant to either a facultative or obligately apomictic plant. Rather, Evans teaches that environment can increase or decrease the amount of apomixis expressed by a facultative apomict.

Hussey, at page 141 in the Summary, teaches:

The frequency at which sexual embryo sacs occur in some facultative apomictic species is influenced by photoperiod. This research was conducted to study changes in the frequency of sexual embryo sacs (SES) in field-grown accessions of buffelgrass [*Pennisetum ciliare* (L.) Link] and to determine the influence of photoperiod on the expression of sexuality under controlled environmental conditions. In a 3-yr field study, mean frequency of SES collected from two facultative buffelgrass accessions (PI 409266 and 409277) ranged from 2.5 to 8.6 percent. Within each year, the greatest number of SES were observed during spring and summer, while a reduction in SES occurred during the late summer and early fall. Under controlled environmental conditions, equal numbers of SES were observed from plants grown at 8, 12, and 16 h. For the two facultative accessions of buffelgrass examined in this study, it was concluded that no relationship existed between photoperiod and frequency of SES under either field or controlled environmental conditions.

Thus, Hussey also teaches that the expression of apomixis in facultative apomicts is influenced by environment. At page 144 of

Hussey, these authors state that their own observations are in agreement with those of Quarin, who noted that conditions that promote maximum flowering responses result in increased frequency of aposporous embryo sacs. Hussey concluded that, in facultatively apomictic buffelgrass accessions, environmental factors other than photoperiod influence the expression of sexuality.

Therefore, the Examiner's statement that "environment causes apospory in many plants" is simply not supported by the references she cited.

For these reasons, withdrawal of the rejection of claims 1, 17-18, and 34-37 for reciting "sexual plants" is respectfully requested.

The Examiner also rejected claims 1, 17-18, and 35-37 for reciting "that are differentiated." The Examiner alleged that it is not clear what this phrase is intended to modify. Applicant respectfully disagrees that this phrase is unclear. After reading the specification, it would be clear to a person skilled in the art that the parental lines are differentiated by their responses to photoperiods and start times and durations of female or seed developmental stages. The interpretation suggested by the Examiner would not necessarily result in selection of the required differences. In view of this, Applicants respectfully assert that

the phrase "that are differentiated" is in compliance with Section 112, second paragraph.

Nevertheless, to advance the prosecution of the application and in furtherance of early allowance of the claims, Applicant has amended the claims to avoid the sentence structure complained of. Withdrawal of the rejection is respectfully requested.

Claims 2 and 3 were rejected for allegedly lacking antecedent basis for "the differentiation in flowering responses." This rejection is moot in view of the amendments to these claims.

Claims 2 and 3 were also rejected for reciting "the differentiation in flowering responses . . . day neutral plants." The Examiner stated that it makes no sense to say that differentiation occurs within short-day plants. This is incorrect. Within the group of short-day plants there are differences in days to flowering and in the length of photoperiod required to induce flowering. See, for example, Salisbury & Ross at 504. Objections to the terms "within" and "across" are moot in view of the amendments.

The Examiner rejected claim 18 for reasons similar to those expressed in the previous paragraph concerning claims 2 and 3. Differences in days to flowering and length of photoperiod required to induce flowering occur even within photoperiodism categories,

which at best are arbitrary delineations of continuously variable phenomena.

Claim 4 was rejected for reciting "differentiation in flowering responses . . . breeding." This rejection is moot in view of the amendment of the claim. A person skilled in the art would recognize that differences can be obtained by selection of pre-existing germplasm or by breeding for the desired characteristics. Therefore, the limitation is not indefinite.

Claims 5-7 were rejected for reciting "differentiation in start times and durations." This rejection is moot in view of amendments to the relevant claims. A person skilled in the art would recognize that the desired traits can be obtained by selection of pre-existing germplasm or by breeding for the desired traits. Therefore, the limitation is not indefinite.

Claim 7 was rejected for reciting "differentiation in start times . . . a breeding step." This rejection is moot in view of amendment of the claim. A person skilled in the art would recognize that desired traits can be selected from pre-existing germplasm or by breeding. Thus, the claim is not indefinite.

Claim 9 was rejected for reciting "lines comprise genomes from each set of delineated lines." This rejection is moot in view of amendment of the claim.

Claim 11 was rejected as lacking antecedent basis for "the genetic material" in line 1. Claim 11 was also rejected for reciting "that confer . . . apomixis." These rejections are moot in view of cancellation of the claim.

Claims 12 and 16 were rejected for allegedly lacking antecedent basis for "said selected hybrid lines." These rejections are moot in view of the amendment to claim 12 and cancellation of claim 16.

Claim 17 was rejected for allegedly lacking antecedent basis for "the hybridization" in part (e). This ground of rejection is moot in view of the amendment to the claim. However, a person skilled in the art would recognize that hybridizing plants necessarily results in a hybridization.

In view of the statement of the applicable law, explanations, and amendments presented herein, it is respectfully submitted that claims 1-9, 11-12, 17-18, 23, and 34-37 are in compliance with the requirements of 35 U.S.C. § 112, second paragraph, and withdrawal of the rejections on that ground is respectfully requested.

VII. Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-9, 11-12, 16-18, 23, and 34-37 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Teletronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). See also, *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). However, a patent need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Determining enablement is a question of law based on underlying factual findings. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

The fact that experimentation may be complex does not necessarily make it undue if such experimentation is typical in the art. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985); *In re Wands*, 858 F.2d at 737,

8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

There are many factors to be considered when making a determination whether or not a disclosure satisfies the enablement requirement and whether or not any necessary experimentation is undue, among which are: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill in the art; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence or absence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement).

It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. MPEP § 2164.01(a). The analysis must consider all of the evidence related to each of these

factors, and any conclusion of nonenablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407.

A. Breadth of the Claims

This invention relates to the intentional production of apomictic plants from sexual parents. While apomixis is known to occur naturally and has been obtained accidentally, prior to the invention of the presently claimed invention, apomixis has not been intentionally obtainable from sexual parents. Apomictic plants can now be intentionally produced by man, for the first time in history, from sexual plants by manipulating variation in photoperiodism, variation in onset and duration of specific seed development stages, and ploidy through conventional plant hybridization, chromosome doubling, and selection procedures. Therefore, this is a pioneering technology, and, as such, the technology is broadly described. The claims have been narrowed considerably to comply with a restriction requirement, which was discussed above. The presently claimed method relates to hybridizing angiospermous plant lines from the same species, genus, or family, wherein the parents are diploids and exhibit differences in responses to photoperiod and female embryological development, and then selecting diploid hybrid progeny that exhibit apomixis. The claims have been limited to diploids merely to comply with the

restriction requirement and in furtherance of early allowance of claims, and not for any other reason.

The Examiner stated that the claims were "broadly drawn to a method of producing apomictic plants from sexual plants by hybridizing any two sets of plant lines" wherein the requisite differences in responses to photoperiod and timing and durations of female or seed developmental stages were present. The claims as presently amended certainly are not that broad, and Applicant asserts that they never were. Applicant never stated or suggested that crosses broader than intrafamily crosses could be successfully carried out. Applicant continually asserted that the parent plants had to be of the same species or closely related plants, which the specification makes clear, and persons skilled in the art would understand, to be within the same genus or family.

In view of the narrow scope of the present claims, Applicant respectfully submits that the breadth of the claims cuts in favor of enablement.

B. Nature of the Invention

This application relates to making hybrid plants. The elected claims relate to making hybrid plants by plant breeding. Plant breeding is a well known technology, and techniques used in the art of plant breeding, such as bagging or emasculation of female

parents, pollination, identification and selection of apomictic hybrids, and the like, are routine and have been used for many years.

It should be recognized that the essential difference between the presently claimed invention and what was previously known in the art is the appropriate selection of parent plants to be used in the hybridization. If parent plants are correctly selected, then the processes of hybridizing the plants and selecting apomictic progeny are identical to processes already well known in the art.

Thus, the nature of the invention also cuts in favor of enablement.

C. State of the Prior Art

Conventional wisdom prior to the filing of the instant specification held that apomixis is caused by an apomixis gene (or two) that is simply inherited. This conventional paradigm is clearly challenged in the present application, although the duplicate-gene asynchrony theory for apomixis (now known as ESDS or embryo sac development sequence) explains why apomixis can appear to be simply inherited. Briefly, apomixis in nature is associated with hybridization and allopolyploidy. Individual chromosomes of allopolyploids are inherited in a simple manner, and this causes apomixis to mimic simple inheritance.

The state of the prior art is to attempt to transfer the supposed one or two apomixis genes into sexual plant lines by breeding with facultative apomictic plants. The present application repudiates the apomixis gene theory and is based on asynchrony of many duplicate genes required for female or seed development. Plant breeding is well known in the art. Any skilled plant breeder would be able to produce apomictic plants if provided with appropriately selected parent plants.

Since the earliest effective filing date of present application, the scientific community has started to shift to a recognition that apomixis is not simply inherited as one or two apomixis genes. Thus, there has been a shift toward the ideas propounded by Applicant. For example, the simply-inherited "apomixis gene" of 8 to 10 years ago (referred to by Koltunow et al., 1995) has now been shown to be a complex genomic region capable of encoding hundreds to thousands of genes and consisting of up to an entire aneuploid chromosome (Ozias-Akins 2003, Sharbel & Mitchell-Olds 2003).

Thus, Applicant respectfully submits that the conclusions of the prior art, namely that apomixis is simply inherited, are incorrect interpretations of what was observed. Plant breeding procedures are well known in the art, as are procedures for recognizing apomixis. Procedures for making embryological

observations of plants are well known in the art. Thus, now that Applicant has taught what to look for when selecting plants to hybridize, any person skilled in the art can make apomictic plants. Hence, the state of the prior art supports a finding that the presently claimed invention is enabled.

D. Level of One of Ordinary Skill in the Art

The level of skill of a person of ordinary skill in the art is relatively high. A person of ordinary skill in the art as of the filing date of the invention would know how to (1) select plants for a plant breeding experiment; (2) recognize different flowering responses to different photoperiods; (3) conduct embryological analyses of plants; (4) hybridize selected sexual plant lines by plant breeding; (5) recover seed from the hybridization, sow such seed, raise plants from such seed, and select hybrid lines from among the progeny; and (6) recognize apomixis in plants.

The high level of one of ordinary skill in the art cuts in favor of enablement. Again, now that Applicant has provided the critical teaching of what to look for when selecting parent plants for hybridization, any person skilled in the art can make apomictic plants.

E. Level of Predictability of the Art

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art, as well as the predictability of the art. In *Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). In other words, the more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention to be enabling. MPEP § 2164.03. Further,

[t]he "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. . . . The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required.

MPEP § 2164.03.

The Examiner alleged that this art is so unpredictable that an enabling disclosure has not been provided for the presently claimed invention. Prior to Applicant's invention, the art was unpredictable because the state of the art was incorrectly understood. A correct understanding of the basis for apomixis, as disclosed in the present application, makes breeding for apomixis predictable. Applicant's Declaration of February 15, 2001, shows that three successes were obtained in three attempts at producing apomictic hybrids in *Antennaria*, *Sorghum*, and *Tripsacum*.

Applicant will now discuss the Examiner's comments concerning this Declaration. First, the Examiner stated that the Declaration does not demonstrate that the specification is enabling for the instantly claimed invention. Applicant respectfully disagrees because in the three examples given in the Declaration, i.e. with the dicot *Antennaria* and two monocots *Sorghum* and *Tripsacum*, apomixis was obtained by following the procedures set out in the specification. In each example, differences in flowering responses to photoperiod and in timing and durations of female developmental stages were identified, and then sexual parent plants were selected and crossed. In each case, the progeny exhibited apomixis.

Second, the Examiner stated that the Declaration teaches that the beginning of embryo sac formation was considered differently in *Sorghum* and *Tripsacum* than it was in *Antennaria*, and that the

specification does not teach this is necessary. Both documents reiterate that the embryological analyses must identify when meiosis and embryo sac formation in divergent lines occurs so that a superpositioning of meiosis and embryo sac formation signals can be produced in hybrids upon hybridization. The methods used to quantify embryo sac formation start times in *Sorghum* and *Tripsacum* could have been used for *Antennaria* and vice versa. Two graduate students working under the direction and tutelage of Applicant in Applicant's laboratory, one working on *Tripsacum* and one working on *Antennaria*, came up with slightly different criteria for evaluating onset times for embryo sac formation. The student working on *Tripsacum* determined that the late tetrad stage in *Tripsacum* is readily observable (so are other stages) and may be slightly earlier than embryo sac formation onset. The student working on *Antennaria* determined that the 2-nucleate embryo sac stage in *Antennaria* is readily observable and is only slightly later than embryo sac formation onset. Both systems work essentially the same and are adequate for angiosperms in general. Both accomplish the task of identifying appropriate parents for hybridization. It is well known in the art that variation exists in plant embryology. This patent application is based in large part on the existence of such variation. A person skilled in the art would expect that certain observations would be more convenient to make in certain

species than in others. It does not require undue experimentation to decide what observations to use in a particular plant. If one follows the guidance provided in the specification, measurements of the timing and durations of embryo sac formation and meiosis compared to the development of nongametophytic structures can be made, regardless of the variation that may be present in a particular species, genus, or family. This is what was done in the three examples described in the Declaration and is what is being done in other species in ongoing work. Thus, the Declaration supports the finding that the specification enables the claims.

Third, the Examiner further stated that the "*Sorghum* crosses in Table 4 show no correlation between differences in photoperiod and the start time and duration of female or seed development and production of apomictic progeny; for example, crosses with plants with no differences in photoperiod produced proportions of apomictic progeny similar to plants with a difference (e.g., hybrids 101 and 76 or 113)." In most biological data sets, one finds exceptions to significant trends. Considering the data set as a whole, which at the time included all available data for *Sorghum*, percentage apomictic embryo sac formation in hybrids was significantly correlated with both photoperiod and dMS (differences in meiosis start times). Means for percentage apomictic embryo sac formation for the 13 hybrids heterozygous for photoperiodism and

the seven hybrids homozygous for photoperiodism were 7.1 and 0.8, respectively, and the analysis of variance was highly significant (Table I). Likewise, the regressions of percentage apomictic embryo sac formation per hybrid (20 total) against dMS (Table II) and ESI-MS (Table III) were significant. Tables 4 and 5 of the declaration demonstrate that apomictic plants can be produced from sexual plants by choosing sexual parents that differ in photoperiodism and in their start times and durations of meiosis and embryo sac formation.

Table I. Analysis of variance table: photoperiodism heterozygosity and percentage apomictic embryo sac formation (means) for the 20 hybrids in Table 4 of Declaration.

Group	Mean	Std. Dev.	SEM		
Photoperiodism heterozygous	7.123	3.550	0.985		
Photoperiodism homozygous	0.786	1.350	0.510		
Power of performed test with alpha = 0.050:0.992					
Source of Variation	DF	SS	MS	F	P
Between Treatments	1	182.738	182.738	20.288	<0.001
Residual	18	162.132	9.007		
Total	19	344.869			
The differences in the mean values among the treatment groups are greater than would be expected by chance; there is a statistically significant difference (P = <0.001).					

Table II. Regression between percentage apomictic embryo sac formation and meiosis start times.

% apomictic ES =  $2.587 + (0.451 * \text{dMS})$ ; N = 20; R = 0.48; Rsqr = 0.23

	Coefficient	Std. Error	t	P	
Constant	2.587	1.317	1.964	0.065	
dMS	0.451	0.194	2.322	0.032	
	DF	SS	MS	F	P
Regression	1	79.470	79.470	5.30	0.032
Residual	18	265.400	14.744		
Total	19	344.870	18.151		

Table III. Regression between percentage apomictic embryo sac formation and ESI-MS (embryo sac initiation - meiosis initiation (see text of Declaration).

% Apomictic ES =  $6.391 - (0.242 * \text{ESI-MS})$ ; N = 20; R = 0.472; Rsqr = 0.223

	Coefficient	Std. Error	t	P	
Constant	6.391	1.083	5.900	<0.001	
ESI-MS	-0.242	0.106	-2.270	0.036	
	DF	SS	MS	F	P
Regression	1	76.764	76.764	5.154	0.036
Residual	18	268.105	14.895		
Total	19	344.870	18.151		

Fourth, the Examiner stated that the "Declaration also teaches that high MS and low EES-MS values are required to produce apomictic progeny (pg 22, paragraph 2); the specification does not teach that this is necessary." High dMS values, as taught in the Declaration, refers to the situation in which there is a large

difference between parents in meiosis start times, which in the specification is taught as a requirement for producing apomictic plants from sexual plants. Low ESI-MS values, as taught in the Declaration, refers to the situation in which embryo sac formation in one parent occurs at about the same time or earlier than meiosis in the other parent. Again, this condition for creating apomictic plants is taught in the specification. The specification and Declaration are consistent in teaching the same requirements for producing apomictic plants from sexual plants. The acronyms dMS and ESI-MS are simply numerical representations that quantify differences in meiosis and embryo sac formation start times and durations based on the maturity level of nongametophytic ovule or ovary tissues, in these cases integument maturity, as is taught in the specification.

Fifth, the Examiner stated that the "Declaration does not teach that apomictic plants could be produced by crossing plants that are not of the same genus." The specification (page 64) teaches that apomictic plants have formed fortuitously through intergeneric hybridizations involving *Hordeum* and *Triticum*; *Triticum*, *Leymus* and *Thinopyrum*; and *Raphanus* and *Brassica* (*Raphanobrassica*). These examples of the fortuitous creation of apomictic plants from sexual plants by crossing plants from different genera demonstrate that the fundamental mechanisms of

producing apomictic plants from sexual plants, as taught in the specification, are not limited by species or genus boundaries. These mechanisms work when parents are of different species or genera or when parents are diploid and/or polyploid.

Applicant will now discuss the references cited by the Examiner.

Garcia et al., 74 Maize Genet. Coop. Newsletter 40-41 (2000) (hereinafter, "Garcia"), was cited as teaching that *Tripsacum* and *Antennaria* have the same type of apomixis. The Examiner alleged that the specification fails to provide evidence that the claimed method would work in plants having different types of apomixis. At page 19, lines 13-16, the specification defines apomixis as those processes routinely resulting in asexual reproduction without conjugation of gametes of opposite sexes (parthenogenesis) from unreduced eggs. At lines 18-21, apomixis is contrasted with polyspory. At page 19, line 11, through page 20, line 5, it is disclosed that apomixis includes the anomalies known as apospory and diplospory. Claim 12 teaches that the anomalies of apospory and diplory, as well as polyembryony, can be produced by the presently claimed methods. John G. Carman's Declaration also reports that the presently claimed methods result in production of aposporic and diplosporic apomicts (e.g., FIG. 7).

The Examiner cited Purnheiser and Dung for allegedly teaching that crossing wheat plants and rice plants, respectively, with different photoperiods and different start times of flowering and different durations of female developmental stages does not produce apomictic plants. Neither Purnheiser nor Dung teaches anything about different start time of flowering and different durations of developmental stages. Purnhauser provides a method for "nicking" wheat plants. "Nicking" plants is a common plant breeding term that refers to methods used to make sure that two plants with different flowering requirements (differences in days-to-flowering or photoperiodism requirements) flower at the same time so that hybrids between them can be made. This paper has nothing to do with cytoembryological divergence (different durations of cytoembryological stages) as defined in the instant specification. Neither of these references discloses the embryological data necessary to draw such conclusions. Thus, this argument is not supportable.

Peel is cited for allegedly teaching that induction of apomixis requires the transfer of alien gene cassettes that confer reproductive asynchrony. Introgression (crossing followed by backcrossing) is only one of several approaches that has been discussed in the literature for attempting to produce apomictic plants (reviewed in the instant specification). The Peel paper

deals with the introgression approach for attempting to convert a sexual crop plant to apomixis. The discussion sections of the Peel papers were largely composed by the Applicant (major professor of the student Peel). These papers were written at the end of the Applicant's 15 year project that was aimed at transferring a single "apomixis gene" (hypothesized mode of regulation of apomixis at that time) from a wild apomictic relative of wheat to wheat by introgression. Shortly before the Peel papers were written, the inventor discovered that apomixis is encoded by unique combinations of divergent alleles from multiple genes that control the onset and duration of different cytoembryological stages. The Peel papers go so far as to define apomixis as a polygenic trait related to such stages. The Peel papers discuss serious complications expected to be encountered in attempting to transfer divergent alleles from multiple genes (gene cassettes) critical to apomixis expression from one species to another. Transferring alien gene cassettes from an apomict to a sexual plant is only a requirement if one chooses to pursue the introgression approach. It is not a requirement of the methods of the patent.

Koltunow is cited as exemplifying the teaching of the prior art that apomixis is caused by a single dominant locus. The specification teaches at page 27, line 23, through page 30, line 2, how the duplicate-gene asynchrony hypothesis explains the many

genomic peculiarities of species exhibiting reproductive anomalies, as well as many inconsistencies of the apomixis literature. As set forth above, apomixis mimics simple inheritance, because individual chromosomes of an allopolyploid are inherited in a simple manner and apomixis in nature is correlated with allopolyploidy, as well as hybridization.

The Examiner further stated that the DeWet article shows that production of triploids means that breeding for apomixis by sexual hybridization is unpredictable. DeWet did not combine parent plants based on cytoembryological divergence as taught in the specification. Hence, the DeWet et al paper is moot.

The Examiner also stated that Applicant agrees with prior Office Action that Hovin, Hanna, and Holm teach that screening of apomictic plants for percentage of apomictic progeny is unpredictable. This is not what Applicant stated. Applicant stated that the Examiner cited several authors from which the Examiner concluded that in the absence of reliable histological, chromosome counting, karyotyping, and progeny test marker techniques the screening of apomictic plants for percentage of apomictic progeny (versus sexual progeny) is unpredictable. Applicant agreed that in the absence of such reliable techniques the screening for apomixis would be unpredictable, however, such techniques are available and well known in the art. Thus,

screening for apomixis is not unpredictable, because all the techniques needed to screen for apomixis are well known. The specification teaches at page 44, lines 3-12, that a combination of embryological investigations and progeny testing is used for verifying expression of apomixis. Embryological investigations are used to determine frequency apomictic embryo sac formation in a putative apomict, i.e. the frequency of ovules on a plant that are developing apomictically. Since the percentage formation of apomictic or sexual embryo sacs does not always correspond to percentage functionality of apomictic or sexual embryo sacs, progeny testing is used to precisely determine the percentage of seeds that were formed apomictically as opposed to sexually. Embryological investigations of a mother apomict may accurately estimate apomictic seed set, especially in apomicts that have high seed set and are highly apomictic already (plants in which most seed are formed apomictically, not sexually). In some apomicts, sexually formed embryo sacs often are not functional; in other apomicts, apomictically formed embryo sacs often are not functional. Hence, it is important to combine embryological testing, which is the only way to determine the type of apomixis being expressed, with progeny testing, which uses morphological and/or molecular markers to identify maternal progeny (those formed by apomixis). Since apomicts are usually highly heterozygous,

morphological progeny testing alone is often very effective in detecting sexually-produced progeny, referred to as off-types (Asker and Jerling 1992, which was incorporated by reference in the specification; see also Bashaw 1980, Apomixis and its application in crop improvement, in Hybridization of Crop Plants, Fehr, Walter and Hadley (eds) Am Soc Agron Publishers, Madison, WI, which was referenced in Asker and Jerling 1992). Molecular markers, which are used to match heterozygosity at numerous loci in the mother apomict with heterozygosity at the same loci in the apomictically-derived progeny, have been used to produce more robust forms of progeny testing (reviewed in Asker and Jerling 1992; see also Bashaw 1980; Barcaccia, Mazzucata, Pezzotti, Falcinelli, 1994, Comparison between isozyme and RAPD analyses to screen aberrant plants in *Poa pratensis* L progenies, Apomixis Newsletter 7: 29-30). Hence, by adding progeny test procedures to embryological analyses, as taught in the instant specification, the problems of screening for apomictic seed set based on embryological analyses alone (as discussed in Hovin, Hanna, and Holm) are effectively overcome. By incorporating the art of progeny testing as taught in the specification, a specific method beyond those taught in the specification is not required for *Sorghum* or for any other species.

The Examiner alleged that the specification does not teach the critical screening methods for determining whether progeny are

apomictic. This is incorrect. The specification teaches these methods at page 44, lines 3-12, and in the references to well know methods, which are also incorporated by reference into the specification.

Thus, the art prior to the Applicant's discoveries were unpredictable because the theories to explain the observations were wrong. Now that correct explanations for the observations have been discovered, the art is not unpredictable, as shown in the specification and Dr. Carman's declaration.

F. Amount of Direction Provided by the Inventor

The application contains a thorough explanation of how the present duplicate-gene asynchrony approach to making apomictic plants is consistent with the observations that have been made in the apomixis field over many years and further explains why the theories and assumptions of the prior art are deficient. At pages 39-44 of the specification are detailed explanations of (a) selection or production of sexual germplasm appropriate for use in producing apomictic plants from sexual plants, (b) hybridization processes used in producing such apomictic plants, (c) amphiploidation processes useful under many circumstances for making apomictic plants, and (d) procedures for verifying expression of apomixis. Examples 1 and 2 at pages 45-51 describe

selecting and collecting germplasm for both dicots and monocots. Examples 3 and 4 at pages 51-55 describe quantifying effects of different photoperiods on flowering for both dicots and monocots. Example 5 at pages 55-57 describes quantifying divergence in female developmental schedules. Example 6 at pages 58-59 describes methods for obtaining greater divergence in female developmental schedules. Examples 7 and 8 at pages 60-62 describe making apomictic plants from sexual lines divergent in floral development.

It should be recognized that the processes of hybridization of selected parent plants and selection of apomictic progeny are well known in the art and have been routine in plant breeding for many years. The critical difference between the presently claimed invention and the prior art is in the identification and selection of parental germplasm. Many of the techniques for identifying such germplasm are already known in the art but, until the present application, had not been used for the presently claimed purposes. With the guidance provided in the present application, it would be a routine matter for a person skilled in the art to select appropriate germplasm and then carry out the hybridization and selection processes for obtaining apomictic plants as claimed.

The Examiner stated that the application fails to provide guidance for methods for hybridizing plants of any two related plant species. Applicant respectfully submits that the Examiner

has incorrectly interpreted related plant species to include "any two plant species." The specification makes clear and it is well known in the art that hybridizations between plants more distantly related than plants of the same family will fail. For example, at page 41, line 19, through page 42, line 9, the specification teaches:

Hybrids are produced between sexual varieties or lines that display appropriate degrees of divergence in photoperiod responses and female developmental schedules. Intraspecific hybrids are made using standard techniques as taught in plant breeding texts, e.g. Poehlman, *Breeding Field Crops* (1987). The successful production of interspecific or intergeneric hybrids may require hormone treatments to the florets and embryo rescue procedures as taught in recent references involving wide hybridization, e.g. Z.W. Liu et al., *Hybrids and Backcross Progenies between Wheat (Triticum aestivum L.) And Apomictic Australian Wheatgrass [Elymus rectisetus (Nees in Lehm.) A. Löve & Connor]: Karyotypic and Genomic Analyses*, 89 *Theor. Appl. Genet.* 599-605 (1994) (incorporated herein by reference).

Poehlman was also incorporated by reference (see page 41, lines 10-11). It also bears pointing out that, to a person skilled in the art, "interspecific" means between species of the same genus and "intergeneric" means between plants of different genera in the same family.

The Examiner also argued that the specification fails to provide guidance for determination of the degree of difference required in flowering responses to photoperiods and female developmental schedules. The specification teaches that

differences in flowering responses to photoperiods include days to flowering after induction thereof (page 47, lines 12-16) and length of photoperiod required to induce flowering (page 30, line 22, through page 33, line 12). Examples 3 and 4 (page 51, line 12, through page 55, line 8) discuss both days to flowering and length of photoperiod required for inducing flowering. Page 40, lines 5-17, teaches that a preferred method of selecting germplasm for producing apomictic plants from sexual plants involves identifying plant of the same species or closely related species that contain ecotypes photoperiodically adapted to broadly-divergent latitudes. Groups of germplasm are selected such that they represent extremes in (a) latitude in which the ecotypes were derived, (b) flowering response to different photoperiods, and (c) timing of female development. At page 33, lines 6-12, the specification teaches that flowering responses to different photoperiods should be distinctly different, and that times and rates of female development should also be distinctly different. Thus, the specification provides significant guidance to a person skilled in the art as to the degree of difference required for parent plants.

G. Working Examples

Compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether a working example is

disclosed. MPEP § 2164.02. The presence or absence of working examples, however, is a factor to be considered.

Example 3 is a working example of quantifying effects of different photoperiods on flowering, with *Antennaria* species used as an example. Example 5 is a working example of quantifying divergence in female developmental schedules, with *Tripsacum* used as an example. FIGS. 3 and 4 of the specification both show actual examples.

Further, additional working examples were provided in the Declaration of John G. Carman Under 37 C.F.R. § 1.132 filed on February 9, 2001. In this Declaration, Dr. Carman disclosed that apomixis was obtained in both dicotyledonous (*Antennaria*) and monocotyledonous (*Sorghum* and *Tripsacum*) plants using the methods described and claimed in the present application. In three attempts, Dr. Carman successfully obtained apomictic hybrids all three times. The Declaration was discussed in more detail above.

#### H. Quantity of Experimentation

Some experimentation will likely be necessary with each new species or genus of plant used in making apomictic hybrids. However, based on the guidance provided in the specification, such experimentation would be merely routine.

Based on all of these factors, the great preponderance of the evidence weighs in favor of an enabling disclosure having been provided. For these reasons, it is respectfully submitted that the requirements of an enabling disclosure under 35 U.S.C. § 112, first paragraph, have been met. Thus, withdrawal of the rejection on this ground is respectfully requested.

VIII. Conclusion

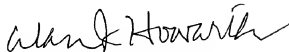
Should the Examiner deem it advisable to conduct a telephone interview for any reason, the undersigned attorney would be most agreeable to receiving a collect telephone call to expedite the prosecution of the application.

For the reasons given above, Applicant respectfully requests reconsideration and allowance of Claims 1-9, 11-12, 17-18, 23, and 34-44 and passage of this application to issue.

Appl. No. 09/576,623  
Amendment dated April 17, 2003  
Reply to Office Action of Nov. 29, 2002

DATED this 21<sup>ST</sup> day of April, 2003.

Respectfully submitted,



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